

AMENDMENT

IN THE CLAIMS:

Please amend the claims as follows:

1-33. (Canceled)

34. (Previously presented) The single molecule reagent according to claim 99, wherein the benzene and X moieties together comprise a member selected from the group consisting of triaminobenzene, tricarboxylbenzene, dicarboxyaniline and diaminobenzoic acid.

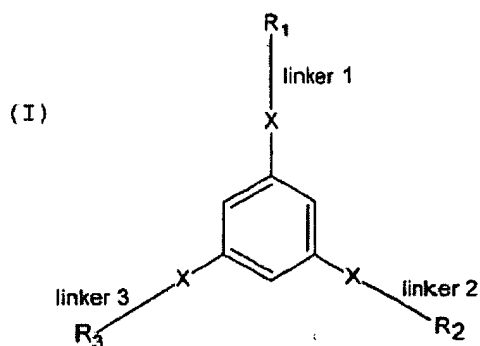
35-72. (Canceled)

73. (Previously presented) A diagnostic composition comprising the single molecule reagent according to claim 99.

74. (Previously presented) A pharmaceutical composition comprising the single molecule reagent according to claim 99.

75-98. (Canceled)

99. (Currently amended) A single molecule reagent for conjugation to a biomolecule with minimal perturbation of said biomolecule, comprising the general structure (I):



wherein each X is a functional group selected from the group consisting of an amino, carboxylic and amide residue;

wherein R₁ is a radionuclide or an affinity ligand selected from the group consisting of biotin, norbiotin, homobiotin, oxybiotin, iminobiotin, desthiobiotin, diaminobiotin, biotin sulfoxide and biotin sulfone having an affinity constant of at least 10^6 M^{-1} to avidin or streptavidin, and is coupled to X in structure (I) via a linker 1;

wherein linker 1 is selected from the group consisting of ethers, thioethers, and ionizable groups comprising carboxylates, sulfonates and ammonium groups, and comprises an aspartyl group;

wherein R₂ is a DTPA derivative or an effector agent selected from the group consisting of radionuclide binding/bonding moieties which are bound via chelation to amino-carboxy derivatives or cyclic amines, said amino-carboxy derivatives or cyclic amines being coupled to X in structure (I) via linker 2;

wherein linker 2 is selected from the group consisting of ethers, thioethers, and ionizable groups comprising carboxylates, sulfonates, or ammonium groups;

wherein R₃ is a biomolecule reactive moiety selected from the group consisting of activated esters, aryl imidates, alkyl imidates, alkyl isocyanates, aryl isocyanates, isothiocyanate, alkyl isothiocyanates, aryl isothiocyanates, maleimides, alpha-haloamides, aryl hydrazines, alkyl hydrazines, aryl acylhydrazines, alkyl acylhydrazines, alkyl hydroxylamines, and aryl hydroxylamines; said biomolecule reactive moiety being coupled to X in structure (I) optionally via a linker 3;

wherein linker 3 is selected from the group consisting of ethers, thioethers, and ionizable groups comprising carboxylates, sulfonates and ammonium groups; and

wherein the X joining benzene to linker 3 can be coupled with linker 3 or, where the linker 3 is absent, the X can be converted directly into the biomolecule reactive moiety.

100. (Previously presented) The single molecule reagent according to claim 99, wherein the biomolecule is a protein or a peptide.

101. (Previously presented) The single molecule reagent according to claim 100, wherein the protein is a monoclonal antibody.

102. (Previously presented) The single molecule reagent according to claim 101, wherein the monoclonal antibody is a tumor binding monoclonal antibody.

103. (Currently amended) The single molecule reagent according to claim 99, wherein ~~R₁~~ is the radionuclide is selected from the group consisting of positron imaging radionuclides, gamma imaging radionuclides and therapeutic radionuclides.

104. (Previously presented) The single molecule reagent according to claim 103, wherein the radionuclide is selected from the group consisting of In radionuclides, Y radionuclides, Pb radionuclides, Bi radionuclides, Cu radionuclides, Sm radionuclides and Lu radionuclides.

105. (Previously presented) The single molecule reagent according to claim 103, wherein the therapeutic radionuclide is selected from the group consisting of Y-90, In-114m, Re-186, Re-188, Cu-67, Sm-157, Lu-177, Bi-212, Bi-213, At-211 and Ra-223.

106. (Previously presented) The single molecule reagent according to claim 103, wherein the gamma imaging radionuclides are Tc-99m or In-111.

107. (Currently amended) The single molecule reagent according to claim 103, wherein ~~R₂ is a~~ the DTPA derivative is selected from the group consisting of Me-DTPA, CICT-DTPA and cyclohexyl-DTPA, or ~~a cyclic~~ the cyclic amine is selected from the group consisting of NOTA, DOTA and TETA, for In, Y, Pb, Bi, Cu, Sm and Lu radionuclides.

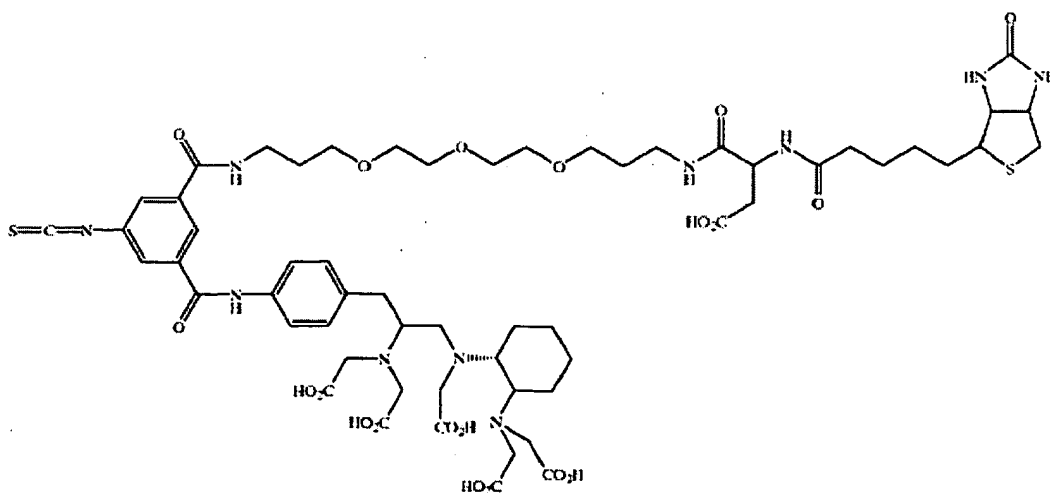
108. (Canceled)

109. (Previously presented) The single molecule reagent according to claim 99, wherein linker 2 and/or linker 3 provides a spacer length of 1 to 25 atoms.

110. (Previously presented) The single molecule reagent according to claim 109, wherein linker 2 and/or linker 3 provides a spacer length of 6 to 18 atoms.

111. (Previously presented) The single molecule reagent according to claim 99, wherein the activated esters are selected from the group consisting of N-hydroxysuccinimide esters, sulfo-N-hydroxysuccinimide esters and phenolic esters.

112. (Previously presented) The single molecule reagent according to claim 99, wherein the reagent is:



113. (Previously presented) The single molecule reagent molecule according to claim 99, wherein the X functional groups to linkers 1 and 2 are amide groups, the affinity ligand is biotin, the effector agent is DOTA, there is no linker to R₃, the X functional group to R₃ is converted directly into an R₃ that is an isothiocyanate.